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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,453	12/19/2005	Mehmet Toner	50254/005002	8260

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EXAMINER	
WARE, DEBORAH K	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
04/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/529,453	TONER ET AL.	
	Examiner	Art Unit	
	DEBBIE K. WARE	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17,24,25,27,44-46,48-50,70-89 and 117-130* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17,24,25,27,44-46,48-50,70-89 and 117-130* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-17, 24-25, 27, 44-46, 48-50, 70-89 and 117-130 are pending.

Response to Amendment

The amendment filed December 4, 2008, has been received and entered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 27, 2008, was filed after the mailing date of the Office Action on May 30, 2008. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

The arguments filed December 4, 2008, have been received and deemed persuasive and the previous art rejection has been removed. However, based upon the arguments and an updated search new art has been discovered and a rejection over the new art has been made on the record as follows:

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 44, 45, 46, 58 and 121-122 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 19, 20-22 and 24 of copending Application No. 11/726,230. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims only differ from the copending claims in terms of the scope of the claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims are drawn to a method of producing a cell population enriched in a first type of cell larger than an adult, enucleated red blood cell via flowing the sample through a device which comprises obstacles.

Copending claims are drawn to a method for producing an enriched cell population comprising a first cell type from a sample comprising two or more cell types via flowing the sample through an array of obstacles.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide for a method for producing a cell population

enriched in a first type of cell as claimed based upon the copending claimed process for producing an enriched cell population because the methods both employ the same step of flowing through a device comprising obstacles and further because the samples to be enriched comprise the same cell types.

The copending claims would have made obvious the instant claims because the same claim features are required by each set of claims. Thus, one of skill would have been motivated to provide for the method of the instant claims based upon a reading of the copending claims with the expectation of successful results. Thus, the claims are rendered prima facie obvious over the copending claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-17, 24-25, 27, 44-46, 48-50, 70-89, 117-130 are rejected under 35 U.S.C. 103(a) as being unpatentable over newly cited Chou et al (USP 7258774) in view of newly cited Nelson et al (US 20020119482) and newly cited Wang et al (USP 7081192), all cited on enclosed PTO-892 Form.

Claims are drawn to methods of producing a cell population enriched in a first type of cell larger than an adult, enucleated red blood cell, comprising the steps of subjecting a blood sample to separation comprising contact with a micro-fluidic device comprising obstacles in a channel separated by gaps so that flow of the blood sample through the device causes cells smaller than the red blood cells and the red blood cells to be directed in a first direction and cells larger than the red blood cells to be directed in a second direction to produce a first sample enriched in larger cells and separation step comprising flowing the first sample through a micro-fluidic device comprising obstacles that bind the fist type of cell in the first sample which produces a population enriched in the first cell type.

Chou et al teach micro-fluidic devices and methods for their use for sorting cells of difference sizes which requires a mechanical control of fluid flow, note abstract and col. 2, lines 5-10. The method comprises steps of subjecting a sample to separation comprising contact with a micro-fluidic device comprising an obstacle or structure to control the flow of the sample through the channel of which is separated by gaps (col. 6, lines 5-12 and col. 17, lines 5-20). The channel is disclosed to be provided with raised protrusions to control flow through the channel, note col. 17, lines 25-40. Also flow can be selectively directed, in a first direction and a second direction, wherein obstacles are

present each having flow channels passing there around or hence having gaps there-between, note col. 22, lines 14-22. Sortable cells include mammalian cells, note col. 30, lines 61-62.

Wang et al teach methods for manipulating moieties in micro-fluidic systems, comprising manipulation which is effected through a combination of a structure that can be external or built-in to the system (see abstract and col. 13, lines 25-35). The moieties can be mammalian cells and red blood cells, including fetal cells in maternal blood from pregnant women, note col. 14, lines 15-20. Micro-fabricated free-standing microstructures are disclosed to be compatible as binding partners (col. 16, line 11 and lines 28-29). Separation is obtainable with the binding partners, note col. 16, line 63. Also note bridging col. 17-18, lines 65-67 and lines 1-13. Further, separation is effected through a combination of the structure with an intracellular moiety, note col. 37, lines 28-46 and lines 52-53. Also any intracellular moiety can be obtained from the target cell-binding complex by any methods known in the art including cell lysis, note col. 38, lines 14-17. Also note col. 41, lines 15-35. The binding partner, which can be structures, are modified with an antibody to aid in the binding, note col. 52, lines 10-12. The structure modified with an antibody encompasses the target cell-binding complex.

Nelson et al teach micro-fluidic method for purification and processing of biologicals. See the abstract. The micro-fluidic device comprises an enrichment channel for cell separation. See the abstract and also note [0099], all lines. The micro-fluidic method comprises a binding separation which makes use of a solid support, note [0103], lines 1-3. Also note [0105], all lines. The separation takes place in the flow

channels, note [0108], [0109] and [0113], all lines and cell lysis is optionally performed. The system is described to include an enrichment process for sorting cells using micro-fluidic device wherein structure combined with capture agents, such as antibody, are used to separate the cell populations from each other.

Claims differ from Chou et al in that cell population separation according to cell size of a blood sample comprising obstacles coated with antibody which can preferentially bind the cells thereby producing a population enriched in cell type larger than an adult, enucleated red blood cell.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to coat the obtacles of Chou et al with the agents and blood sample disclosed by Wang et al and Nelson et al in order to produce a cell population enriched in cells larger than an adult, enucleated red blood cell. The micro-fluidic device is clearly suggested, if not taught, by the cited prior art combination.

One of skill in the art as taught by Chou et al would have been motivated to preferentially bind the cells to the obstacles as disclosed by Want et al and Nelson et al because Chou et al clearly disclose that cellular material can stick to flow channel sidewalls which makes enrichment of a cell population using such devices problematic. Thus, to selectively bind the cells to the obstacles would have been expected to overcome this problem in the art and provide a successful result.

Clearly there is a suggested in the art to provide for a micro-fluidic device comprising obtacles that preferentially bind cells to produce a population enriched in a certain desirable cell type from blood cells. Fetal cells in particular can be sorted and separated this way from a blood sample, as taught by the cited prior art. Blood samples would have been expected to contain adult, enucleated red blood cells as well as other cells which are smaller and larger than these red blood cells.

Releasing the cells bound to the obstacles is clearly suggested to include cell lysis and/or shear force. Arraying, staining cells and analyzing cells (e.g. FISH, DNA analysis), the cells is also well within the purview of an ordinary artisan. Furthermore, to control the amount of bound cells is also within the skill of an artisan because preferential binding using antibodies is well recognized and an appropriate antibody can be selected which can control the percentage amount of bound cells to the obstacles.

The obstacles are clearly suggested, if not taught, to be capable of being orderly formed in a pattern or two-dimensional array. Also anti-CD45 antibody is clearly a matter of judicious selection and well known in the art. In addition, to select a diluent after lysis for purposes of diluting the cell lysis product comprising NaHCO3 and acetazolamide is also an obvious modification of the cited prior art and well within the purview of an ordinary artisan to do in order to optimize conditions and control the percentage amount of bound cells to the obstacles. In

the absence of persuasive evidence to the contrary the claims are clearly *prima facie* obvious over the cited prior art.

All claims fail to be patentably distinguishable over the state of the art discussed above and cited on the enclosed PTO-892 and/or PTO-1449. Therefore, the claims are properly rejected.

The remaining references listed on the enclosed PTO-892 and/or PTO-1449 are cited to further show the state of the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DEBBIE K. WARE whose telephone number is (571)272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information

system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah K. Ware/
Deborah K. Ware
Examiner
Art Unit 1651